



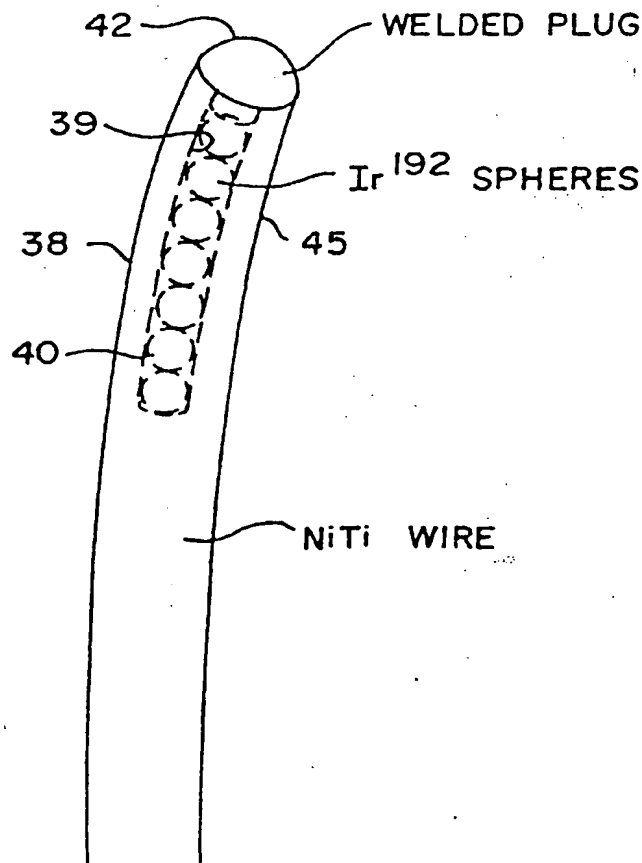
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(54) Title: RADIOACTIVE SOURCE WIRE, APPARATUS AND TREATMENT METHODS

(57) Abstract

A source wire (38) having a radioactive source (40) at its distal tip (45) is used to treat tissue at a target site within a patient's body by localized in vivo radiation. The source wire (38) is advanced to the target site along a pathway such as an implanted catheter (12) or a natural vessel or duct of the patient's body from a point external to the body. The source wire (38) may be a solid lead of substantially uniform thickness along its entire length, composed of nickel titanium alloy having desired characteristics including flexibility, springiness, slipperiness, mechanical strength and shape memory retention. Instead, the wire (38) may be a cable composed of multiple strands of substantially uniform thickness throughout the entire length of each strand. In either case, the distal end (45) of the overall wire (38) is tapered for ease of entry into the narrower portions of the pathway.



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# RADIOACTIVE SOURCE WIRE, APPARATUS AND TREATMENT METHODS

## Background of the Invention

The present invention relates generally to radioactive sources used for treatment of tissue in the human body. More particularly, the invention resides in a device, apparatus, and methods for treating tissue by irradiation with a predetermined dose from a radioactive source which is delivered into the body of the patient via a natural or artificial pathway for a very brief treatment interval or fractionated treatment sessions. The device, apparatus and methods of the invention are especially well suited for brachytherapy in which a malignant tumor is exposed to localized in vivo radiation from a pathway within or adjacent the tumor site, or for controlled irradiation of the wall of a blood vessel, particularly coronary arteries or related blood-carrying canals, to condition the interior surface thereof against restenosis.

Brachytherapy, a technique for radiation treatment of malignant tumors, attacks the tumor from within the body. The method typically utilizes a radioactive source wire in which a radioisotope sealed at and substantially integral with the distal tip of a relatively thin wire or cable is delivered via a pathway formed by a catheter or through a natural cavity, duct or vessel of the body directly to the tumor site for localized irradiation. One or more catheters, for example, may be implanted in the patient's body to provide the pathway(s) from a point external to the body to and through the tumor site, so that the interior of

the tumor mass is accessible via the catheter(s). The radioactive source, with a dose that may range from about one curie to about ten curies, is mechanically delivered to the site either by hand feeding the source wire (for low  
5 dose and more readily accessible tumor sites) or by means of apparatus known as an afterloader which has a drive system to which the proximal end of the source wire is connected.

Usually, the treatment is fractionated, in that repeated short intervals of treatment are performed, with  
10 the source wire being introduced for the irradiation, left in place for the predetermined interval prescribed by the attending oncologist (often after consultation with a physicist who has calculated the size of the tumor, the distance to be traveled by the source, the nature of the  
15 pathway to be traversed and likely travel time, and other pertinent factors), and then withdrawn into the afterloader's shielded safe. To permit treatment to be performed through multiple catheters to the tumor site, if deemed appropriate by the oncologist, the afterloader may be  
20 provided with a turret for automatic delivery of the source wire in succession to the entry points of the several catheters for automated advancement, treatment and withdrawal in each pathway. The desired treatment time in each case is programmed into the afterloader's control unit.

25 The treatment regime may be repeated at regular intervals over a period of many days, weeks or months, and, if successful, results in complete destruction or at considerable shrinkage of the tumor(s). Among the

advantages of this type of radiation therapy are exposure of the tumor to fractionated treatment doses of localized radiation so that each individual treatment need only be of extremely short duration to provide the desired effect while  
5 reducing the extent of patient exposure and discomfort, and to provide relatively rapid shrinking of the tumor while avoiding prolonged exposure of healthy tissue to radiation.

Because this type of therapy is more applicable to inoperable malignancies deep within the body, the site of  
10 the tumor(s) is usually difficult to reach as the source wire is guided through the path provided by the implanted catheter. The catheter itself may be positioned in place using a previously implanted guidewire or "rail" over which it is advanced along a lumen distinct from the lumen of the  
15 catheter through which the source wire is advanced and retracted. It is often the case that this pathway is long, extremely narrow and tortuous with numerous bends and turns. It is essential, therefore, that the source wire should be suitably thin, strong and flexible to traverse the pathway.  
20 Furthermore, the wire must be adapted to carry a suitably sized radioactive source, i.e., the core which, for high dosage treatments, is typically substantially pure iridium processed in a neutron flux to produce the radioactive isotope Ir-192. Hence, the source wire has the conflicting  
25 requirements that it be of sufficiently small diameter and flexibility to traverse the path to and from the tumor, sufficiently strong along with its flexibility to be driven through the pathway without binding or kinking during wire

advancement, and with the capacity to deliver a radiation dosage of as much as ten or more curies.

Prior art source wires include cable composed of a multiplicity of tiny strands of stainless steel wire to provide both desired strength and flexibility, but which lack the size or diameter to travel through the smallest sizes of pathways required for brachytherapy treatment of certain tumors, such as in or through the biliary tract or the bronchi of the lungs. Also, cable source wires typically require welding a plug or capsule containing the radioactive source to the distal tip, which creates a point of weakness where fracture may occur. It is imperative, of course, that the source wire be sufficiently sound and reliable to avoid even the remote possibility that it may break and cause the radioactive material portion to be left in the patient's body for a protracted interval of time.

Solid source wire is capable of accommodating the Ir-192 or other source material in a hole formed in the distal tip of the wire to provide better sealing and security of the source material. Also, solid source wire can be produced by specialized techniques in sizes ranging down to from about 0.6 to 0.7 millimeter (mm) diameter to accommodate an Ir-192 source having a dosage or radioactive level or strength of up to about 10 curies. Other conventional source materials include cobalt, cesium, palladium, gold, and iodine. The source wire may be composed of stainless steel, platinum or certain other conventional materials of suitable flexibility.

For low dose sources in particular, such as one curie or slightly higher, the source material may be installed and the entire source wire then subjected to processing in a nuclear reactor to impart the desired level of radioactivity to the source material. This is an acceptable procedure where the half-life of the wire material is considerably less than that of the source material, so that the radioactivity of the wire material itself is sufficiently dissipated to permit it to be used within a few days after activation. Platinum wire, for example, is suitable for that purpose. For higher dose sources, the source material alone is subjected to the neutron flux and subsequently assembled in the wire by means of shielded, remotely controlled handling and manipulating techniques.

Recently, it has been found that radioactive irradiation of the interior wall surface of blood vessels in general and the coronary arteries in particular with a low dose source for a very brief interval following treatment of the vessel for removal or compression of occluding material such as plaque, enjoys marked success in preventing restenosis. Restenosis is a recurrence of the stricture or narrowing of the vascular lumen or heart valve following surgery or other treatment for removal or reduction of an occlusion, or from related trauma. For example, cardiac patients who have been treated by balloon angioplasty, artery interior wall scraping, laser removal of plaque, bypass surgery, and other conventional techniques for treating

stenosis or occlusion of the blood vessels either because of or in avoidance of myocardial infarction, have been found to experience high incidence of restenosis.

Approximately one-third of the patients who have had arteries unblocked suffer restenosis about six months later, requiring that the procedure be redone. And in fact, repeating the procedure appears to increase the trauma to the smooth muscle cells and to speed their regrowth. Fifty percent of the patients experience some form of reocclusion of the treated vessel. While a repeat procedure may not be required for all of those patients, some reocclusion does occur. The remaining 50% of the patients seem to suffer no reocclusion, and there is no single explanation for it.

The fact that one-third of all patients require retreatment, at substantial additional cost and with potential loss of life raises questions concerning the significance of a 95% success rate for the initial unblocking procedure. Moreover, if a second reocclusion occurs, the next procedure performed on the patient is likely to be open heart surgery.

Restenosis, then, is really an injury response mechanism to the unblocking procedure, at least for some substantial percentage of the patients. Attempts to correct the restenosis problem by use of drugs have not been successful.

Irradiation of the vessel wall with a radioactive source appears to alleviate the problem in tests conducted on rabbits and rats, but creates a new problem in that the



source wire must be sufficiently thin, flexible and strong to be capable of placement in the offending arteries. This is by no means a simple task, because of the small size of the vessels, the difficulty in reaching the target area through the artery as a consequence of the small size of the target and the tortuous pathway involved, and especially the susceptibility of the patient to a heart attack if the critical vessel is blocked for an inordinate time during performance of the treatment.

10           The problems involved are similar to, if not greater than, those encountered in treatment of tumors by brachytherapy as described above. It is a principal object of the present invention to provide new and improved source wires, apparatus and methods for in vivo, localized, internal radioactive treatment of selected tissue in the human body.

          The cost of treatment for heart attack victims is staggering, and is among the procedures being addressed in a strong effort toward cost containment by treatment centers and other care providers. Of course, if treatment is unsuccessful, inadequate or untimely, the cost is even greater -- in loss of life. Therefore, it is another important object of the present invention to provide improved and lower cost means and methods for treating cardiac patients to avoid restenosis of the veins and arteries, and even of the heart valves, following procedures

used to open a blocked or partially blocked or inoperative blood passageway.

#### Summary of the Invention

According to the present invention, a new and improved radioactive source wire is provided for use both in brachytherapy and cardiac treatment for the purposes described above. In particular, the source wire is composed of a nickel-titanium alloy known commercially as nitinol which has the desired properties of flexibility, springiness, slipperiness, mechanical strength and super-elasticity, and which returns to a straight shape after it is withdrawn from the narrow tortuous pathway through which it was driven for purposes of treatment. The radioactive source material, such as Ir-192 (iridium isotope) spheres, is loaded in an axial hole in the distal tip of the wire, which is then sealed with a nitinol plug as by welding. The nitinol source wire is readily returned to the drive system of the afterloader without likelihood of kinks or bends, for subsequent use in another or other procedures of the same type.

The wire is composed of a shape memory alloy, the nickel/titanium alloy nitinol being preferred, possessing super-elastic properties and the capability, at proper temperature, of transforming from an unstressed austenitic state (being a straight configuration) to a stress induced martensitic state and the capability of returning to the austenitic state when the externally induced stress is

removed. The deformations encountered in tortuous pathways are fully recovered without permanent plastic deformation, and the material transforms to the stable austenitic state for storage or spooling with no permanent deformation from the prior use.

Nitinol has been used commercially in bendable frames for lenses (eyeglasses). It has also been used in the past for rails (guidewires) that are employed in various parts of the body by placement through a lumen to define a selected site as a means to transport and retrieve items to and from that site. In this way, the rail dispenses with the need to relocate the the selected site repeatedly, such as for placement of catheters. However, to our knowledge, there has been no suggestion that nitinol would serve a useful purpose as a source wire for radioactive source material.

The procedure for which the nitinol source wire is used may be a brachytherapy application or a coronary radiotherapy application. The same basic afterloader drive system is used for both applications, although the machines themselves are somewhat different. For example, the brachytherapy (oncology) afterloader is more complex only because of the large variety of targets (tumors at sites possibly anywhere in the body, versus targets at or in the region of the heart for the coronary machine), and up to about 20 channels versus only one channel required for the coronary radiotherapy machine. The radioactivity shielded safe is larger on the oncology machine because the source is

of greater radioactivity level. Also, in the coronary machine it is not necessary to use a turret, or at maximum, a two-position turret, whereas the turret of the brachytherapy afterloader has a number of positions corresponding to the array of channels available for delivery of treatment. The basic structure of each machine may be entirely conventional.

In the coronary radiotherapy treatment procedure of the invention, the afterloader equipment is adapted to advance a dummy wire (non-radioactive) through the implanted catheter to the target site under visual observation such as fluoroscopy, after which the dummy wire is retracted, and the source wire is then automatically advanced to the target site through the catheter for localized irradiation of the vessel wall over a very brief period of time that depends on the radioactivity dosage prescribed by the attending physician. The dummy wire has an opaque tip marker to facilitate the fluoroscopic observation, and the precise location of the target area along the pathway is calibrated in the afterloader according to the measured distance of travel by the dummy wire. The treatment is performed automatically by remote operation of the afterloader which is located in a radiation-shielded room where the patient is placed for the treatment.

A treatment catheter is coupled to the end of the afterloader connector and deployed over a rail guidewire to the target site for ultimate delivery and retraction of the radioactive source. In the case of coronary radiotherapy,

the source material in the source wire must be centered to provide uniform irradiation to achieve maximum results. A non-centered source could deliver too little radiation to one side of the artery interior wall, resulting in no effective treatment of that region, and too much to the other side, resulting in possible injury to that portion.

#### Summary of the Drawings

The above and still further objects, features and attendant advantages of the present invention will become apparent from consideration of the following detailed description of certain presently preferred embodiments and methods of the invention, taken in conjunction with the accompanying drawings, in which:

FIG. 1 is a simplified view of a typical arrangement for implementing a procedure with a brachytherapy system or a coronary radiotherapy system according to the present invention;

FIG. 2 is a fragmentary, perspective view of a catheter, rail, and source wire connected at the proximal end to the afterloader drive connector;

FIG. 3 is a simplified side view of the system of FIG. 2;

FIG. 3A is a sectional view through the lines A-A of FIG. 3; and

FIG. 4 is a fragmentary sectional side view of the source wire showing an exemplary assembly of the radioactive

source material and special wire material according to the invention.

Detailed Description of the Preferred Embodiment and Method

Referring to FIG. 1, the invention in one of its  
5 aspects is used in treatment regimens provided by a  
brachytherapy system or a coronary radiotherapy system. In  
practice, the patient 10 is moved into a radiation-shielded  
treatment room where the procedure will be performed. A  
treatment catheter 12 is implanted in the patient, and, in  
10 the coronary or cardiac procedure is also coupled to a  
connector of the drive system for the remote afterloader 15.  
The drive system, and indeed, the entire afterloader may be  
completely conventional for the brachytherapy application,  
and would require only a few changes for the cardiac  
15 application.

It will be understood that while both uses are  
described in this specification, in the typical case, the  
patient will go through only one of the two procedures.  
Also, separate afterloaders and treatment rooms would be  
20 provided for the two different applications. The description  
of both procedures here is solely for the sake of  
convenience, and because many aspects of the present  
invention are applicable to both types of treatment.

For treatment, the patient 10 is placed in a  
25 supine or a prone position on a table 17, with the  
afterloader 15 placed in close proximity to allow the source  
wire of the afterloader to be deployed through the treatment

catheter into the selected target site in the patient's body. The afterloader is controlled by the attending physician, an oncologist in the case of brachytherapy treatment or a cardiologist in the case of cardiac treatment, and/or by a radiotherapist 20 from a control console 22. In practice, the control console may be in the treatment room where low dose radioactivity treatment is being performed, but shielded with the attendant by a set of radiation screens 25, or may be located outside the shielded treatment room for high dose radioactivity treatments.

A fluoroscope 28 is positioned above the patient, although its use would usually be required only for the cardiac treatment. A video camera and display monitor 30 are positioned to allow attendant 20 to view the patient, with equipment including display controls 31 positioned within easy access to the attendant.

The method used in performing brachytherapy is entirely conventional, and hence, only portions of it will be described here in those portions of the text where appropriate. Description of the method and certain specialized apparatus employed for the cardiac treatment will be described presently. First, however, it is desirable to describe aspects and features of the preferred embodiment of a source wire which, except for radioactive dosage requirements, may be used for either procedure.

According to the preferred embodiment of the invention, the source wire is an assembly of an elongate wire composed of a nickel/titanium alloy commercially

marketed as nitinol. Nitinol is available, for example, from Shape Memory Alloys of Sunnyvale, California. The material is described, for example, in U.S. Patent No. 4,665,906. For purposes of the source wire application according to the invention, the nitinol in the form of a wire is stored in its austenitic state (below the transition temperature, discussed below), characterized by a straightened shape, and when used is flexed to put it in a stress-induced martensitic state (above the transition temperature), which is characterized by super-elasticity. When the wire is formed, the process, which involves several separate treatments at high temperature, produces a transition temperature of the material between its austenitic state in which it is ductile, to the stress-induced martensitic state. In source wire of the invention, the nitinol is always used for treatment at a temperature above the transition temperature, which is typically  $15^{\circ}\text{C} \pm 5^{\circ}\text{C}$ , for example, and is in the austenitic state except when the wire is in flexation at which it is in the stress-induced martensitic state. This is the case for the nitinol wire used in either of these applications, where it is bent and flexed as it moves through a tortuous path in the human body in the brachytherapy treatment or cardiac treatment procedure.

The transition temperature may be varied somewhat as a function of the manner in which the nitinol wire is processed, especially its heat treatment. For example, in one form in an austenitic state the wire material was



floppy, which did not adversely affect cycling tensile strength or shear strength. In the preferred form the nitinol wire has a sufficient memory aspect to retain straightness despite a capability to be

5           For purposes of assuring retention of its desired properties in that state, such as the properties of high flexibility, springiness, slipperiness and mechanical strength, the nitinol wire is heat treated while it is being processed to form wire of the desired diameter for use in  
10 the brachytherapy and coronary radiotherapy applications of the invention. As with stainless steel rods and wires, nitinol can be drawn and successively redrawn to progressively smaller diameters.

          Because the manufacturing process can affect the  
15 wire's properties, it is important to verify metallurgical specifications as part of the testing of the wire for performing validations, including basic factors such as ultimate tensile strength. Cycling of the wire (i.e., putting it through tests in which it is used and reused in  
20 the intended manner for the application) is important to detect otherwise unseen characteristics that may adversely affect its performance, such as case hardening due to grinding, and to assure absence of lot-to-lot variations.

          Three different processes were employed to produce  
25 the nitinol wire for use in source wire according to the invention. It was necessary both to produce the wire in its final form (i.e., dimensional including diameter and length) and to provide it with a cavity in which radioactive source

material would be retained. In particular, an axial hole is formed at the distal end of the wire to house the source material, which would subsequently be sealed to prevent particulate loss and contamination.

5           One process of producing the wire with an axial hole at its tip involved drilling a hole in an oversize wire or rod, followed by repeated drawing of the wire through progressively smaller dies until the desired wire diameter and hole depth were achieved. During the drawing stages the  
10   depth of the hole underwent lengthening, as would be expected, so it is necessary to calculate the desired final depth and from that, determine the depth of initial drilling of the hole. Wire diameter of 0.023 inch and hole diameter  
15   of 0.014 inch is preferred. This hole drilling and drawing process to provide the final form of the wire and desired properties was performed for the assignee of the present application by the Raychem Corporation of Menlo Park, California.

          A second process, also performed by Raychem  
20   Corporation, produced a similar form of wire which constitutes a thin-walled nitinol tube clad over a nitinol backbone wire running substantially the entire length of the tube except for a portion at the tip. This portion provides the hole of desired depth to house the source material.  
25   Other dimensions of the tube/backbone wire are substantially the same as those described above for the drilled hole/drawdown version of the wire. A slightly greater outer diameter of 0.022 inch resulted from this process.

A third process, which was used only to produce the axial hole in the tip of a nitinol wire of the final desired diameter, involved the use of electrical discharge machining (EDM) performed by Mega Technology EDM, Inc. of Norcross, Georgia. In contrast to the other processes, the EDM process has tended to produce a hole wall of somewhat varying thickness. In any event, however, the EDM process did produce a hole of desired diameter and depth in the end of the wire without need for further drawing.

A fragmentary portion of the final source wire is shown in the side sectional view of FIG. 4. The nitinol elongate wire 38 with axial hole 39 in its distal tip is loaded with radioactive source material such as iridium isotope Ir-192 spheres 40 of slightly smaller diameter than that of the hole 39. The radioactivity level of the total source material in the wire is preferably about one to two curies (a low dose wire) for the cardiac application, and from that dose up to about 10 curies (a high dose wire), depending on physician-prescribed dosage, for the brachytherapy application.

After loading the source material, a nitinol plug 42 of preferably rounded shape is inserted into hole 39 to tightly cap it. The plug is then welded to seal the hole against loss of any source material. The source material may be enriched Ir-192, and in any event is substantially pure iridium converted to radioactive form by treatment in a nuclear reactor in a known manner. The radioactive spheres are assembled in the nitinol wire and the hole is

sealed with the welded plug by manipulations performed using remote manipulators in an assembly area.

A feature of the preferred embodiment of the source wire is that it may be tapered down at the distal end to provide even greater flexibility in reduced size at the point of delivery of the dosage to the target which is to be irradiated. A somewhat larger diameter of the wire up to the point at which the taper begins is useful to provide the column strength sufficient for drivability of the wire by the afterloader. For example, in the embodiment of FIG. 4 the distal end 45 of the wire may be tapered over the last six inches to the tip, by drawing that portion through an appropriately sized die. The tapering process would be performed prior to loading radioactive source material.

If a multi-strand cable were used in place of a solid wire for the source wire, the cable can similarly be tapered. This is accomplished by tapering every strand at the distal end, so that when the strands are twisted to produce the final form of the cable, it has a rat-tail shaped taper. Although it is not the preferred mode of a source wire, the multi-strand cable form may be assembled with a small capsule containing the radioactive source material, by welding the capsule to the distal tip of the cable. Each strand may have an extremely small cross-section, e.g., 0.001 inch, so that it bends easily, making the overall cable very flexible. Such cables have been produced without taper in stainless steel, but a form used

in accordance with the present invention would employ nitinol strands.

By way of comparison, a nitinol solid wire has almost twice the column strength of a multi-strand stainless steel cable of corresponding diameter. Multiple strand cable ordinarily has a slight advantage in flexibility, but the nitinol material tends to reduce that advantage by virtue of its flexibility, even as a solid lead. Such flexibility is especially important in the applications described herein. Insufficient flexibility can cause the wire to develop small kinks as it travels through curves in the catheter, and the kinks become of greater width in any short section of the wire than the width of the catheter lumen. Consequently, the wire will lock in the catheter, perhaps so much so that it becomes immovable in either direction. This is completely unacceptable where a radioactive source wire is being used.

In the method of the invention, a treatment catheter 12 (FIGS. 1, 3) is implanted in the patient to provide the pathway to be traveled by the source wire, and the wire is advanced (or withdrawn) in that pathway through the catheter during the treatment procedure, whether for brachytherapy or for coronary radiotherapy. Of course, the selected target is different depending upon application.

In the cardiac application, the catheter is also coupled to the afterloader connector 50 by a guidewire or rail 52 which extends to the target site. The catheter for that application may be provided with small channels to

allow some blood flow therethrough. The catheter 12 is placed over the rail 52 which is hooked into the connector for the afterloader as well. The afterloader connector 50 is also coupled to the turret. A key 55 is used to lock the coupling in place and prevent the catheter and the rail from undergoing rotation.

Since the rail lumen 58 (FIG. 3A) is at the top of catheter 12, the key 55 on the afterloader coupling 50 locks the catheter against rotation. If the catheter were allowed to rotate, the rail (guidewire) 52 would begin uncontrollable spinning because of the eccentricity of its lumen 58 in the catheter. Orientation of the guidewire channel is also extremely important, and is maintained by the key.

The cardiac application of the radioactive source wire is extremely size sensitive. Among critical issues for that application are flexibility for access through the fine and tortuous pathways to the very fine and remote blood vessels, and size for entry into the vessels.

A suitable level of radioactivity (dosage) for the source in this application is one curie, and such a source would be kept in place a period sufficient to produce, say, 1,000 to 1,500 rads at one millimeter distance from the vessel or valve wall. Radioactivity delivered to the wall surface depends on factors such as the length of source, the length of the lesion and the curie level on the day the treatment is performed, and the length of time of the treatment.

The patient can only tolerate one to one and a half minutes of total occlusion in the target area, which means that the treatment must be stopped before the limit is reached, the attending personnel then return, the balloon is  
5 deflated to allow the heart (or the portion being treated) to reoxygenate. After an interval of, say, three to five minutes, the treatment procedure is recommenced to apply the remaining dosage required to irradiate the target area by redeployment of the source wire and the centering balloon.

10 It is also imperative to provide centering of the wire in the vessel, although somewhat less so with a small diameter artery because, for example, one side may be  $2\frac{1}{2}$  mm and the other may be 2 mm. The need to center exists to avoid a hot spot on one side. Preliminary results also  
15 indicate that a failure to obtain a certain threshold of radiation on the vessel wall, about 1,000 rads, will result in no discernible prevention of restenosis.

In the preferred embodiment, an inflatable balloon is provided in the catheter for centering the source tip of  
20 the source wire. A dose of 1,000 to 1,500 rads drops off according to the inverse square of the distance, so that a distance of 5 mm from the vessel wall to the source (actually the tip of the source wire), causes the field strength to drop off sharply, with concomitant loss of threshold. The  
25 treatment catheter may include, in addition to the working treatment (radiotherapy) channel, the rail (guidewire) channel, an inflation channel for the centering balloon. Segmented or scalloped balloons, or otherwise channeled

balloons may be used, together with a channeled catheter or alone, to permit some flow-by of blood sufficient to avoid complete blockage during treatment.

For treatment at the bottom of the heart, a  
5 scalloped catheter with no balloon is preferred. In that situation, centering of the source within that treatment area with some blood flow-by capability is achievable without need for a balloon.

A different type of centering mechanism may be  
10 used, and in that event could be of a type and shape that would permit sufficient blood flow so that the procedure need not be stopped before the treatment regimen is completed. The problem of using a different mechanism is principally in the means for deployment. Balloon inflation  
15 and deflation in a catheter is in and of itself an entirely conventional technique and has a proven record of safety.

The irradiation procedure is preferably performed very soon after the balloon angioplasty (PTCA) or other unblocking procedure is completed on the vessels. The rail  
20 (guidewire) is left in place during the period of treatment because it allows a rapid return to the target. Since the rail is tiny, at 0.014 inch, it does not seriously impede blood flow. Initially, the rail is steered into the part of the heart being targeted, using a fluoroscope, becomes the  
25 first component in and the last out.

If not installed properly, a branching effect can occur. Thus, the catheter and subsequently the source wire must be advanced to the desired branch via the rail. The



catheter is placed over the rail, and in available size ranges, is capable of moving through vessels or ducts as small as two mm in diameter.

5 Lumen diameter of the artery dictates the choice of treatment catheter as well as the radioactivity dose. If it is determined that the dose should be 1,450 rads, for example, that value is entered on the control console of the afterloader, or other factors may be entered by which a microprocessor in the control console may calculate the dose  
10 according to location of the target, size of lumen, center of the lumen (distance to the interior wall surface), curie rating per day, and other known factors.

A fail-safe function of the afterloader senses patient problems when the coronary radiotherapy is adminis-  
15 tered. In the event that the patient is experiencing pain or other difficulties, the source wire is promptly drawn back and the balloon is deflated and the patient's heart is allowed to reoxygenate. The target location is marked with a dummy wire deployed from the afterloader. The control  
20 console of the afterloader enables programming of the desired functions. A one to one and one-half minute interval is timed by the afterloader, the procedure halted at that point, the source wire is retracted into the safe. The afterloader retains all necessary data such as the dose  
25 given and the dose given on transit to and from the point at which initiated, or transit dose, and treatment is re-commenced after a break of two or three minutes.

Although a preferred embodiment and method of the present invention has been described herein, it will be apparent from the foregoing description to those skilled in the field of the invention that variations and modifications of the invention may be implemented without departing from the spirit and scope of the invention. Accordingly, it is intended that the invention shall be limited only to the extent required by the appended claims and the rules and principles of applicable law.

WHAT IS CLAIMED IS:

1           1. A source wire for treating tissue within a  
2 patient's body by localized in vivo radiation of tissue at  
3 a target site from a radioactive source of the source wire,  
4 the source wire being introducible by applicator to the  
5 target site via an implanted catheter or a natural vessel,  
6 duct or chamber of the patient's body that provides a  
7 pathway or portion of a pathway to the target site from a  
8 point external to the body, said source wire comprising:

9           an elongate wire composed of nickel-titanium  
10 alloy, having preselected properties of flexibility,  
11 springiness, slipperiness, mechanical strength and shape  
12 memory retention, said elongate wire having a proximal end  
13 and a distal end, and

14           a radioactive source assembled with said elongate  
15 wire at the distal tip thereof for delivery through said  
16 pathway to the target site by loading and advancing the  
17 elongate wire along the pathway from the proximal end of the  
18 elongate wire, until the source is disposed at the target  
19 area for irradiating the selected tissue.

1           2. The source wire of claim 1, wherein:

2           the elongate wire is a solid lead of substantially  
3 uniform thickness along its entire length.

1           3. The source wire of claim 1, wherein:

2           the elongate wire is a cable composed of a  
3 multiplicity of strands of substantially uniform thickness  
4 throughout the entire length of each strand, each strand  
5 having a distal end and a proximal end.

1           4. The source wire of claim 3, wherein:  
2           the distal end of at least some of the strands is  
3 set back relative to the distal end of the elongate wire and  
4 to the distal end of other strands of the cable, to form a  
5 taper that narrows from a point short of the distal end of  
6 the wire to the distal end of the wire, for ease of entry  
7 into portions of the pathway of reduced size.

1           5. The source wire of claim 2, wherein:  
2           the elongate wire has an axial hole of  
3 predetermined depth at its distal tip,  
4           the source is disposed in said axial hole, and  
5           a plug is fastened to the distal tip of the  
6 elongate wire to seal said axial hole with the source  
7 disposed therein.

1           6. The source wire of claim 5, wherein:  
2           the source comprises an iridium isotope that has  
3 been irradiated to a predetermined radioactivity level for  
4 treatment of the tissue in the target area.

1           7. The source wire of claim 6, wherein:

2 the source comprises a plurality of segments of  
3 said iridium isotope.

1 8. The source wire of claim 6, wherein:  
2 the iridium isotope has a radioactivity level of  
3 at least one curie.

1 9. The source wire of claim 6, wherein the tissue  
2 to be treated is a malignant tumor, and  
3 the iridium isotope source has a radioactivity  
4 level of approximately 10 curies.

1 10. The source wire of claim 9, wherein:  
2 the elongate wire has a diameter less than  
3 approximately 0.028 inch.

1 11. The source wire of claim 6, wherein the  
2 tissue to be treated is an interior surface of a vascular  
3 wall which has been subjected to trauma by prior treatment  
4 to reduce the presence of plaque, and  
5 the iridium isotope source has a radioactivity  
6 level in the range of approximately 1 to 2 curies.

1 12. The source wire of claim 11, wherein:  
2 the elongate wire has a diameter less than  
3 approximately 0.021 inch.

1 13. The source wire of claim 1, wherein:

2           the elongate wire is an assembly of a tube and a  
3   solid backbone wire running the entire length of the tube  
4   except for a displacement of the end of the backbone wire  
5   relative to the same end of the tube to form an axial hole  
6   of predetermined depth to accommodate radioactive source  
7   material therein, and

8           a plug fastened over the open end of the axial  
9   hole to securely seal the source material therein.

1           14.   A method of treating smooth muscle cell  
2   tissue within the body of a patient, using a radioactive  
3   source wire, comprising the steps of:

4           implanting a catheter in the patient to provide a  
5   pathway from a point external to the patient's body to a  
6   point at or near a predetermined target area about the  
7   patient's heart for the tissue to be treated,  
8           advancing a source wire including an elongate lead  
9   having a distal end with a radioactive source thereat and a  
10   proximal end from which the source wire is advanced, through  
11   the catheter by limiting the elongate lead to a sufficiently  
12   small diameter to carry the radioactive source to the  
13   immediate vicinity of the tissue for irradiation thereof in  
14   the target area, having selected the elongate lead to be  
15   sufficiently flexible and mechanically strong to traverse  
16   the catheter without substantial kinking while resisting  
17   breakage,

18           halting the advance of the source wire through the  
19 catheter when the distal end reaches the point at which the  
20 source wire is to irradiate tissue in the target area,  
21           irradiating the targeted tissue for a  
22 predetermined interval of time, and  
23           withdrawing the source wire from the catheter  
24 immediately upon completing the irradiation of tissue for  
25 the duration of the interval.

1           15. The method of claim 14, wherein the target  
2 area is a coronary artery, and further including:  
3           centering the distal tip of the source wire in the  
4 coronary artery to produce substantially uniform irradiation  
5 of the radioactive tissue adjacent the source,

1           16. The method of claim 15, further including:  
2           performing the irradiation substantially  
3 immediately after the coronary artery has been subjected to  
4 opening of the lumen by reduction of the thickness of plaque  
5 on the interior surface of the wall of the artery, to  
6 produce substantially uniform irradiation of the radioactive  
7 tissue adjacent the source, and thereby reduce the  
8 likelihood of restenosis of the irradiated interior surface  
9 of the artery wall.

## AMENDED CLAIMS

[received by the International Bureau on 19 September 1994 (19.09.94);  
original claims 1-5, 10 and 12-16 amended; new claims 17-45 added;  
remaining claims unchanged (16 pages)]

1                   1.    A source wire for treating tissue within a  
2    patient's body by localized in vivo radiation of selected  
3    tissue at a target site from a radioactive source of the  
4    source wire, the source wire being introducible to the  
5    target site via an implanted catheter or a natural vessel,  
6    duct or chamber of the patient's body that provides a  
7    tortuous pathway or portion thereof to the target site from  
8    a point external to the body, said source wire comprising:  
9                   a thin elongate member composed of nitinol  
10   selected to maintain an austenitic state characterized by a  
11   normally straight shape capable of a predetermined degree of  
12   flexation while traversing said tortuous pathway and to be  
13   stress-induced by flexation within said predetermined degree  
14   to a martensitic state characterized by super-elasticity,  
15   with a transition temperature above which said member is  
16   transformed from said austenitic state to said martensitic  
17   state when said member is stressed and below which no  
18   stress-induced martensitic state will be formed, said  
19   transition temperature being preselected to be below the  
20   patient's body temperature, so that said member will remain  
21   in the austenitic state during positioning, treatment by,  
22   and withdrawal of the radioactive source except for portions  
23   of the member while flexed and thereby temporarily stress-  
24   induced to the martensitic state during advancement to and  
25   withdrawal from said target site, said elongate member  
26   having a proximal end and a distal tip, and



27           a radioactive source assembled at the distal tip  
28 of said elongate member for delivery through said tortuous  
29 pathway to the target site by loading and advancing the  
30 elongate member from the proximal end thereof until the  
31 distal tip thereof is disposed at the target area with the  
32 radioactive source positioned for irradiating the selected  
33 tissue.

1           2.    The source wire of claim 1, wherein:  
2           the elongate member is a solid lead of substan-  
3           tially uniform thickness along its entire length.

1           3.    The source wire of claim 1, wherein:  
2           the elongate member in its overall length compris-  
3           es a cable composed of a multiplicity of strands of substan-  
4           tially uniform thickness throughout the entire length of  
5           each strand, each strand having a distal end and a proximal  
6           end.

1           4.    The source wire of claim 3, wherein:  
2           the distal ends of respective strands of the cable  
3           are offset rearward relative to the distal tip of the cable  
4           by successively greater amounts in the direction from the  
5           cable center to the cable exterior, to form a tapered array  
6           of strands near and up to the distal tip of the cable, for  
7           ease of entry of the distal tip of the cable into portions  
8           of the tortuous pathway of reduced size relative to the size  
9           of other portions of the pathway.

1                   5.    The source wire of claim 2, wherein:  
2                   the elongate member has an axial hole of predeter-  
3   mined depth at its distal tip,  
4                   the radioactive source is disposed in said axial  
5   hole, and  
6                   a plug is fastened to the distal tip of the  
7   elongate member to seal said radioactive source within said  
8   axial hole.

1                   6.    The source wire of claim 5, wherein:  
2                   the source comprises an iridium isotope that has  
3   been irradiated to a predetermined radioactivity level for  
4   treatment of the tissue in the target area.

1                   7.    The source wire of claim 6, wherein:  
2                   the source comprises a plurality of segments of  
3   said iridium isotope.

1                   8.    The source wire of claim 6, wherein:  
2                   the iridium isotope has a radioactivity level of  
3   at least one curie.

1                   9.    The source wire of claim 6, wherein the tissue  
2   to be treated is a malignant tumor, and  
3                   the iridium isotope source has a radioactivity  
4   level of approximately 10 curies.

1           10. The source wire of claim 9, wherein:  
2           the elongate member has a diameter less than  
3           approximately 0.028 inch.

1           11. The source wire of claim 6, wherein the  
2           tissue to be treated is an interior surface of a vascular  
3           wall which has been subjected to trauma by prior treatment  
4           to reduce the presence of plaque, and  
5           the iridium isotope source has a radioactivity  
6           level in the range of approximately 1 to 2 curies.

1           12. The source wire of claim 11, wherein:  
2           the elongate member has a diameter less than  
3           approximately 0.021 inch.

1           13. The source wire of claim 1, wherein:  
2           the elongate wire is an assembly of a tube and a  
3           solid backbone wire running the entire length of the tube  
4           except for a displacement of the end of the backbone wire  
5           relative to the same end of the tube to form an axial hole  
6           of predetermined depth to accommodate radioactive source  
7           material therein, both the tube and the backbone wire being  
8           composed of nitinol, and  
9           a plug fastened over the open end of the axial  
10          hole to securely seal the source material therein.

1           14. A method of treating smooth muscle cell  
2 tissue within the body of a patient, using a radioactive  
3 source wire, comprising the steps of:

4           implanting a catheter in the patient to provide a  
5 pathway from a point external to the patient's body to a  
6 point at or near a predetermined target area about the  
7 patient's heart for the tissue to be treated,

8           advancing a source wire including an elongate lead  
9 having a distal end with a radioactive source thereat and a  
10 proximal end from which the source wire is advanced, through  
11 the catheter by limiting the elongate lead to a sufficiently  
12 small diameter to carry the radioactive source to the  
13 immediate vicinity of the tissue for irradiation thereof in  
14 the target area, the elongate lead being composed of nitinol  
15 which has been treated to maintain an austenitic state  
16 characterized by a normally straight shape capable of a  
17 predetermined degree of flexation while traversing the  
18 pathway provided by the catheter and to be stress-induced by  
19 flexation within said predetermined degree to a martensitic  
20 state characterized by super-elasticity, with a transition  
21 temperature above which said member is transformed from said  
22 austenitic state to said martensitic state when said member  
23 is stressed and below which no stress-induced martensitic  
24 state will be formed, said transition temperature being  
25 preselected to be below the patient's body temperature, so  
26 that said lead remains in the austenitic state during  
27 positioning, treatment by, and withdrawal of the radioactive  
28 source except for portions of the lead while flexed and

29 thereby temporarily stress-induced to the martensitic state  
30 during advancement to and withdrawal from said area, thereby  
31 maintaining the source wire sufficiently flexible and  
32 mechanically strong to traverse the catheter without  
33 substantial kinking while resisting breakage,

34 halting the advance of the source wire through the  
35 catheter when the distal end reaches the point at which the  
36 source wire is to irradiate tissue in the target area,

37 irradiating the tissue over a predetermined length  
38 of the target area for a predetermined interval of time, and

39 withdrawing the source wire from the catheter  
40 immediately upon completing the irradiation of tissue over  
41 said predetermined length for the duration of the time  
42 interval.

1 15. The method of claim 14, wherein the target  
2 area is within a coronary artery, and further including:

3 centering the radioactive source of the source  
4 wire to a maximum practicable extent in the lumen of the  
5 coronary artery toward providing substantially uniform  
6 irradiation of the tissue in a predetermined band of  
7 efficacy about the source in each segment of the predeter-  
8 mined length of the target area.

1 16. The method of claim 15, further including:

2 performing the irradiation of tissue substantially  
3 immediately after the predetermined length of the target  
4 area of the coronary artery has been treated to unblock the

5 artery lumen, the irradiation being of a preselected dosage  
6 to reduce the likelihood of restenosis of the irradiated  
7 interior surface of the artery wall.

1 17. An intravascular radiation therapy method of  
2 precluding the proliferation of smooth muscle cell tissue  
3 along a preselected portion of the length of the interior  
4 surface of a coronary artery of a patient which has been  
5 subjected to treatment and resulting trauma by a procedure  
6 for unclogging the lumen of the coronary artery along said  
7 preselected portion of its length, comprising the steps of:  
8 inserting and advancing a thin elongate member  
9 through the vascular system of the patient from a proximal  
10 end of the member external to the patient's body, to  
11 position a radioactive source of predetermined radioactivity  
12 level affixed at a distal end of the member within said  
13 preselected portion of the length of the coronary artery,  
14 centering said radioactive source of the member to  
15 a maximum practicable extent in the lumen of the coronary  
16 artery to subject tissue along each segment of said  
17 preselected portion of the length to a radiation dosage in  
18 a circumferential cross-sectional band about the source  
19 encompassing the artery wall, and constituting a  
20 predetermined therapeutic range of efficacy over a predeter-  
21 mined time interval of therapy, to prevent restenosis in  
22 said preselected portion of the length of the coronary  
23 artery, and

24                withdrawing the distal end of the member from the  
25        patient's vascular system after tissue along the entire said  
26        preselected portion of the length of the coronary artery has  
27        been subjected to said radiation dosage in said prede-  
28        termined therapeutic range.

1                18. The method of claim 17, further including:  
2                maintaining said radioactive source of the member  
3        generally centered in the lumen of the coronary artery by  
4        inflating a centering balloon adjacent the distal end of  
5        said member before positioning said radioactive source at a  
6        selected location in said preselected portion of the length  
7        of the coronary artery.

1                19. The method of claim 17, including:  
2                using a thin elongate member composed of nitinol  
3        which has been treated to maintain an austenitic state  
4        characterized by a normally straight shape capable of a  
5        predetermined degree of flexation while traversing the  
6        patient's vascular system and to be stress-induced by  
7        flexation within said predetermined degree to a martensitic  
8        state characterized by super-elasticity, with a transition  
9        temperature above which said member is transformed from said  
10       austenitic state to said martensitic state when said member  
11       is stressed and below which no stress-induced martensitic  
12       state will be formed, said transition temperature being  
13       preselected to be below the patient's body temperature, so  
14       that said member remains in the austenitic state during the

15 positioning, treatment by, and withdrawal of the radioactive  
16 source except for portions of the member while flexed and  
17 thereby temporarily stress-induced to the martensitic state  
18 during advancement to and withdrawal from said preselected  
19 portion of the length of the coronary artery.

1 20. The method of claim 17, including:  
2 using as said thin elongate member a solid wire,  
3 with the radioactive source sealed within a hole formed in  
4 the tip of the distal end of the wire.

1 21. The method of claim 17, including:  
2 selecting said radioactive source to have a  
3 radioactivity level in a range from less than one curie to  
4 about two curies.

1 22. The method of claim 17, including:  
2 selecting said member to have a predetermined  
3 portion at its distal end which is tapered to a diameter  
4 substantially smaller than the lumen of the coronary artery  
5 in at least said preselected portion of the length thereof,  
6 from a substantially uniform diameter of the member along  
7 the remainder of its entire length from the proximal end  
8 thereof to the point of commencement of the tapered portion,  
9 to ease entry of the member into a typically narrowed said  
10 preselected portion of the length of the coronary artery.



1           23. The method of claim 17, including:  
2           inserting and advancing a catheter in the  
3 patient's vascular system along a guide wire eccentrically  
4 disposed in the lumen of the catheter to said preselected  
5 portion of the length of the coronary artery, as a pathway  
6 for advancement and withdrawal of said member.

1           24. The method of claim 23, including:  
2           holding the catheter and guide wire against  
3 rotation in the patient's vascular system.

1           25. The method of claim 17, including:  
2           maintaining the radioactive source generally  
3 centered in the lumen of the coronary artery in each segment  
4 of said preselected portion of the length for said predeter-  
5 mined interval of time to produce a radiation dosage to  
6 tissue in said predetermined therapeutic range of efficacy  
7 over said predetermined time interval in a range from about  
8 1,000 to 1,500 rads at a distance of one millimeter from the  
9 surface of the radioactive source.

1           26. The method of claim 18, including:  
2           deflating the centering balloon periodically to  
3 allow reoxygenation of the patient's heart after brief  
4 intervals of the radiation therapy.

1           27. The method of claim 26, including:

2                withdrawing said member from the patient's  
3                vascular system after deflating the centering balloon to  
4                preclude overdosage of radiation to tissue during each  
5                period of reoxygenation of the patient's heart.

1                28. The method of claim 18, including:  
2                selecting the centering balloon to be segmented,  
3                scalloped, or otherwise channeled to permit blood flow  
4                during intervals of the radiation therapy.

1                29. The method of claim 23, including:  
2                providing a centering balloon for the radioactive  
3                source in the catheter, with the centering balloon being  
4                inflatable and deflatable via a lumen of the catheter.

1                30. The method of claim 17, including:  
2                advancing and withdrawing said member into and  
3                from the patient's vascular system by means of a remote  
4                afterloader.

1                31. Apparatus for intravascular radiation therapy  
2                to preclude proliferation of smooth muscle cell tissue along  
3                a preselected portion of the length of the interior surface  
4                of a coronary artery of a patient after such portion has  
5                been subjected to treatment and resulting trauma by a  
6                procedure for unclogging the lumen of the coronary artery  
7                along said preselected portion of its length, said apparatus  
8                comprising:

9           a thin elongate member adapted to be advanced  
10 through the vascular system of the patient from a proximal  
11 end of the member external to the patient's body,

12           a radioactive source of predetermined radioactivi-  
13 ty level affixed at a distal end of the member for  
14 positioning within said preselected portion of the length of  
15 the coronary artery, and

16           centering means for centering said radioactive  
17 source of the member to a maximum practicable extent in the  
18 lumen of the coronary artery to subject tissue along each  
19 segment of said preselected portion of the length to a  
20 radiation dosage in a circumferential cross-sectional band  
21 about the source encompassing the artery wall and  
22 constituting a predetermined therapeutic range of efficacy  
23 over a predetermined time interval of therapy, to prevent  
24 restenosis in said preselected portion of the length of the  
25 coronary artery.

1           32. The apparatus of claim 31, wherein:

2           said centering means comprises an inflatable  
3 centering balloon disposed adjacent the distal end of said  
4 member.

1           33. The apparatus of claim 32, wherein:

2           said centering balloon includes channels to permit  
3 blood flow past the balloon during intervals of the  
4 radiation therapy.

1                   34. The apparatus of claim 32, wherein:  
2                   said centering balloon is segmented to permit  
3 blood flow in the artery during intervals of the radiation  
4 therapy.

1                   35. The apparatus of claim 32, wherein:  
2                   said centering balloon is channeled to permit  
3 blood flow in the artery during intervals of the radiation  
4 therapy.

1                   36. The apparatus of claim 31, wherein:  
2                   said centering means comprises a centering balloon  
3 for the radioactive source, and a catheter having a lumen  
4 for inflating and deflating the centering balloon.

1                   37. The apparatus of claim 31, wherein:  
2                   said thin elongate member is composed of nitinol  
3 selected to maintain an austenitic state characterized by a  
4 normally straight shape capable of a predetermined degree of  
5 flexation while traversing the patient's vascular system and  
6 to be stress-induced by flexation within said predetermined  
7 degree to a martensitic state characterized by super-  
8 elasticity, with a transition temperature above which said  
9 member is transformed from said austenitic state to said  
10 martensitic state when said member is stressed and below  
11 which no stress-induced martensitic state will be formed,  
12 said transition temperature being preselected to be below  
13 the patient's body temperature, so that said member will

14 remain in the austenitic state during the positioning,  
15 treatment by, and withdrawal of the radioactive source  
16 except for portions of the member while flexed and thereby  
17 temporarily stress-induced to the martensitic state during  
18 advancement to and withdrawal from said preselected portion  
19 of the length of the coronary artery.

1 38. The apparatus of claim 31, wherein:  
2 said thin elongate member comprises a solid wire,  
3 in which said radioactive source is sealed within a hole in  
4 the tip of the distal end of the wire.

1 39. The apparatus of claim 31, wherein:  
2 said radioactive source has a radioactivity level  
3 in a range from less than one curie to about two curies.

1 40. The apparatus of claim 31, wherein:  
2 said member has a predetermined portion at its  
3 distal end which is tapered to a diameter substantially  
4 smaller than the lumen of the coronary artery in at least  
5 said preselected portion of the length thereof, from a  
6 substantially uniform diameter of the member along the  
7 remainder of its entire length from the proximal end thereof  
8 to the point of commencement of the tapered portion, to ease  
9 entry of the member into a typically narrowed said pre-  
10 lected portion of the length of the coronary artery.

1           41. The apparatus of claim 31, further including:  
2           a guide wire adapted to be affixed in the patients  
3   vascular system, and a catheter adapted to be inserted and  
4   advanced into the patient's vascular system along the guide  
5   wire, to provide a pathway for advancement and withdrawal of  
6   said member.

1           42. The apparatus of claim 31, further including:  
2           means for holding the catheter and guide wire  
3   against rotation in the patient's vascular system.

1           43. The apparatus of claim 31, wherein:  
2           said thin elongate member is a nitinol wire.

1           44. The apparatus of claim 31, further including:  
2           a remote afterloader for advancing and withdrawing  
3   said member into and from the patient's vascular system.

1           45. Apparatus for intravascular radiotherapy of  
2   a patient, comprising:

3           wire means adapted to be advanced through the  
4   vascular system of the patient from a point external to the  
5   patient's body,

6           radioactive core means having a predetermined  
7   level of radioactivity and secured to an end of the wire  
8   means which is to be advanced into and withdrawn from the  
9   patient's vascular system, and

10 means for generally centering the radioactive core  
11 means at a point in the patient's vascular system which is  
12 to receive said radiotherapy, so that tissue at said point  
13 of the vascular system will receive radiation dosage in a  
14 band between a smaller and a larger circumference about said  
15 point representing a predetermined therapeutic range of  
16 efficacy over a predetermined time interval of the  
17 radiotherapy.

## STATEMENT UNDER ARTICLE 19

Claims 1-5, 10, and 12-16 have been amended and new claims 17-15 have been added to the provide protection of which applicant's invention is deemed deserving in light of the dearth of prior art that could be considered to anticipate or render obvious the invention. U.S. Patent 5,199,939 to Dake et al. (Dake) is cited by the International Bureau as being particularly relevant to claims 14-16 in that the claimed invention cannot be considered novel in light of the invention disclosed in Dake. Neither Dake, nor any other reference cited, however, discloses, teaches, or suggests centering the radioactive material in the artery, much less a satisfactory technique for doing so. As taught in the applicant's specification, positively positioning the radioactive source material substantially at the radial center of the coronary artery is essential to achieve substantially uniform irradiation of the tissue in the artery wall. Failure to center the source adequately will result in the source likely being too close to one side of the artery wall, with consequent injury to the tissue proximal to the radiation source from overexposure and a corresponding ineffective treatment of the tissue distal to the source.

As amended, method claims 14-16 now require the substantial centering of the source material. Additionally, these claims require use of an elongate member composed of the super-elastic alloy nitinol. As amended, apparatus claims 1-13 also are restricted to the use of nitinol. Super-elastic nitinol withstands a high degree of deflection without permanent deformation and therefore is able to traverse tortuous pathways to and in the coronary arteries without buckling or kinking while resisting breakage. Neither the use of nitinol for this purpose, nor the characteristics or properties selected for the material found to be particularly suitable for intravascular radiotherapy, or the provision of such material with an affixed radioactive core, are found in the prior art, and certainly not in the references of record. It should be emphasized that the provision of a nitinol source wire with an integral or incorporated radioactive source is itself a significant achievement, at least because the techniques that might be thought suitable to achieve that end



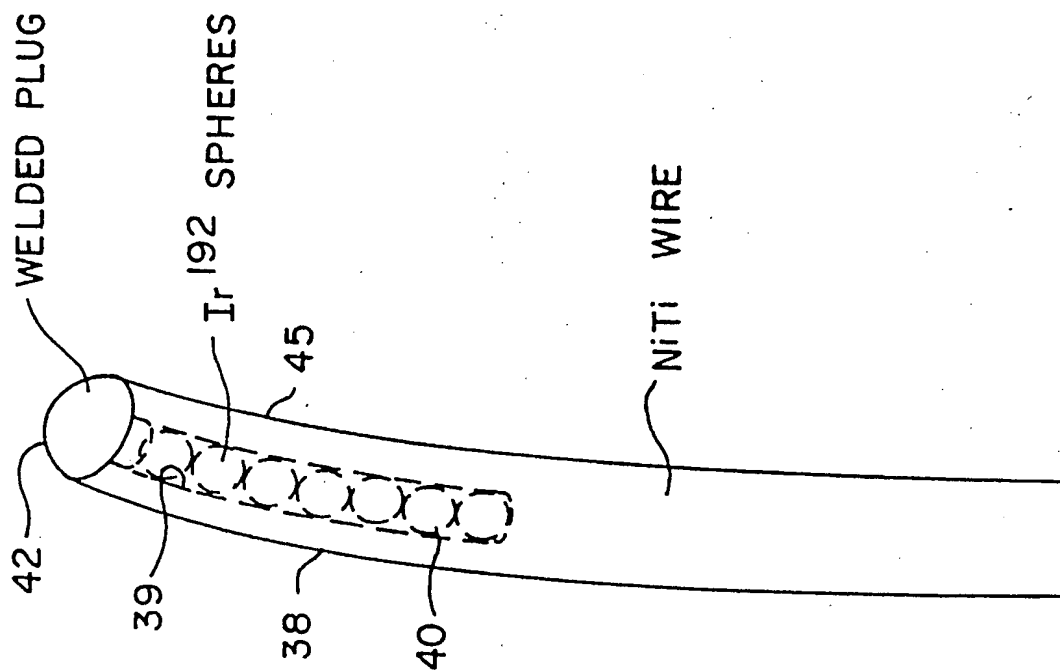


FIG. 4

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(5) :A61N 5/00 US CL :600/001 According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 128/772; 600/001-008				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched NONE				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) NONE				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	US, A, 5,199,939, (DAKE ET AL.), 06 April 1993. See entire document.	14-16		
Y	US, A, 5,084,002, (LIPRIE), 28 January 1992. See entire document.	1-13		
Y	US, A, 5,111,829, (ALVAREZ DE TOLEDO), 12 May 1992. See entire document.	1-13		
Y	US, A, 4,861,520, (VAN'T HOOFT ET AL.), 29 August 1989. See entire document.	5-13		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; border: none;">           * Special categories of cited documents:            "A" document defining the general state of the art which is not considered to be part of particular relevance            "E" earlier document published on or after the international filing date            "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)            "O" document referring to an oral disclosure, use, exhibition or other means            "P" document published prior to the international filing date but later than the priority date claimed         </td> <td style="width: 50%; vertical-align: top; border: none;">           "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention            "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone            "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art            "&amp;" document member of the same patent family         </td> </tr> </table>			* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be part of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
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Date of the actual completion of the international search 23 JUNE 1994		Date of mailing of the international search report JUL 19 1994		
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